A CASE OF STRYCHNINE POISONING.

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J. B., aged forty-nine years, was admitted to the University Hospital on November 14, 1911, suffering from chronic lymphatic leukemia. He was a large, powerful man, weighing 190 pounds stripped. On December 5, at 8.15 A.M., he received through error 15 grains of strychnine sulphate in three capsules. At 9.15 A.M. I was sent for hurriedly. The patient was found rigidly extended on his bed, conscious, and extremely apprehensive that some terrible thing was about to befall him. He complained of intense pain in the back of the neck. From time to time his muscular rigidity increased suddenly, and he repeatedly asked to be held on the bed for fear that he should throw himself off. He was immediately given a quarter of a grain of morphine and preparations were made to wash out the stomach. A few minutes later, on attempting to pass the tube, it was found that the patient could not separate his teeth by more than half an inch. The trismus rapidly increased, the jaws became rigidly shut, and the patient passed into a severe tonic convulsion with cessation of respiration. During this he became intensely cyanotic, the pulse was very small, rather rapid, high tension, and with frequent intermissions, apparently due to the occurrence of extrasystoles. A probable diagnosis of strychnine poisoning was made at this time. Efforts made to open the mouth with a gag during the convulsion were unavailing, and resulted in loosening several teeth. One-tenth grain of apomorphine was injected. Shortly after, the stomach tube was successfully passed through a nostril and the stomach thoroughly washed out. The patient vomited repeatedly during this washing and the vomitus contained milk curds. The washing was repeated at 9.50 A.M., 10.20 A.M. and 11.00 A.M., and on each occasion there was vomiting. A second severe general convulsion occurred at 10.00 A.M. Shortly after this chloroform anesthesia was started. This was changed to ether at about 11.00 A.M., and the patient was kept continuously under the anesthetic until 4.30 P.M. An enema containing forty grains of sodium bromide and twenty grains of chloral hydrate was given at 10.30 A.M. No further severe general convulsions occurred but milder convulsive movements were noted at 11.00, 11.30 A.M., 12.00 M., and 12.25, 12.40 and 12.50 P.M. Other milder convulsive movements were not recorded. These mild convulsions were frequently precipitated by the patient's efforts to talk, by attempts to move him, by noises, etc. They occurred especially when the anesthesia became lighter. They consisted of momentary periods of extreme stiffening of the trunk and extremities, and they were usually accompanied by involuntary cries and expressions of pain. They did not produce cyanosis. As it was felt that an indefinite quantity of the strychnine might have passed into the intestines, two drops of croton oil were placed on the tongue at 9.40 A.M., and this dose was repeated at 12.45 and 3.00 P.M. No bowel movement, however, occurred until evening; 123 c.c. of urine were obtained by catheter at 1.30 P.M. and 390 c.c. at 6.25 P.M. Thereafter micturition was voluntary. At 5.45 P.M. a pint of saline solution, with 10 grains of diuretin, was given by rectum, and this was repeated about once in two hours until noon of the following day. A flood of urine and numerous small stools were passed during the night. Repeated twitchings of the muscles were noted up to midnight. On the following morning the patient complained of soreness of the muscles, which persisted for several days. For several nights he was restless, and complained of muscular twitchings. On December 10 he developed a severe stomatitis, which lasted about ten days. No definite cause for this could be found, but it was supposed to be due either to an infection following the injury to his teeth or to the local irritant effect of the croton oil. He left the hospital on January 1, 1912, with no evident remaining effect of his experience.

This case is noteworthy because of the amount of strychnine taken (15 grains). The fatal dose is commonly stated to be ½ to 1½ grains, although according to Gadamer it is considerably higher (2 to 6 grains[1]). Over 1⅗ grains were recovered from the urine of our patient. Much larger doses taken by the mouth have of course been recovered from under prompt treatment; even from such exceptional doses as 75 grains, 60 grains, and 20 grains. The dose taken by our patient stands among the large ones on record. His recovery was due in part to the presence of food in the stomach, which retarded the passage of the poison into the intestines and in part to the prompt emptying of the stomach at the onset of symptoms; 4½ grains were obtained from the first stomach washings, but unfortunately, the later washings were not analyzed.

The case is interesting on account of the attempt to determine quantitatively the amount of strychnine excreted in the urine and the rate of excretion. Examination of the urine of fatal cases of poisoning have usually shown only minimal amounts and frequently none at all (Masing and Dragendorff[2]). Lesser[3] found traces in only 2 of 5 fatal cases. Kratter[4] found it in the urine of a man who died in one and a half hours. On the other hand medicinal doses of this drug appear promptly in the urine. Mann found it in thirty minutes,[5] Kratter in thirty-five minutes, Rautenfeld in two hours, and Hale[6] in two to three hours. The excretion continues for one[7] to four days,[8] or possibly longer. In animals it may appear very promptly in the urine. Ipsen[9] found it in two and one-half minutes in rabbits and five minutes in dogs. Rapmund[10] found it in four minutes in rabbits.

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[1] The literature of strychnine poisoning has been carefully summarized by E. Rapmund, Vierteljahrschr. f. gerichtl. Med., 1911, xlii, 243; E. Allard, Vierteljahrschr. f. gerichtl. Med., 1903, xxv, Suppl. 234; R. Kobert, Lehrbuch der Intoxikationen, Zweite Auf., 1906, 1153.

[2] Quoted in Allard, loc. cit., 299.

[3] Vierteljahrschr. f. gerichtl. Med., 1898, xv, 269.

[4] Wien. med. Woch., 1882, xxxii, p. 214.

The specimens of urine from our patient were carefully saved and sent to the hygienic laboratory of the University of Michigan, where the analyses were made under the direction of Dr. V. C. Vaughan. From each specimen 100 c.c. of urine were evaporated to dryness on the water-bath. The residue was extracted with 100 c.c. of alcohol and again evaporated to dryness on the water bath. This residue was dissolved in 100 c.c. of water. It was then made feebly alkaline with ammonia and shaken in a separating funnel with 100 c.c. of chloroform. The chloroform was evaporated to dryness and the residue was again taken up in slightly acidulated water, again made alkaline with ammonia, and again shaken out with chloroform. The residue from this last chloroform extraction was rubbed up with a few drops of concentrated sulphuric acid and heated for one-half hour on the water bath. It was again dissolved in water, to which ammonia was again added, until the solution was slightly alkaline. It was then shaken out with chloroform, the chloroform was evaporated to dryness, and the residue weighed.

The results of the analyses of the urine of our patient are shown in the following chart. Unfortunately no analyses were made of the urine which was passed between 6.05 A.M. on December 6 and that which was passed at 2.30 P.M. on December 7.

ANALYSES OF URINE AFTER TAKING 1.0 GRAM STRYCHNINE AT 8.15 A.M. ON DECEMBER 5, 1911.

Time passed.	Amount of urine in c.c.	Specific gravity.	Albumin.	Strychnine in grams.	Average per hour.	
					Amount urine.	Strychnine.
December 5, 1.30 P.M. . .	123	.....	......	0.0010	23	0.0002
6.25 P.M. . .	290	1.001	Positive	0.0200	58	0.0040
11.30 P.M. . .	500	1.010	......	0.0490	100	0.0098
December 6, 1.15 A.M. . .	350	1.009	......	0.0105	200	0.0060
2.55 A.M. . .	220	1.007	......	0.0110	120	0.0060
3.45 A.M. . .	185	1.009	......	0.0027	200	0.0032
6.05 A.M. . .	300	1.009	......	0.0019	125	0.0007
December 7, 2.30 P.M. . .	290	.....	......	Trace		
December 8, 24-hour specimen		.....	......	Faint trace		
December 9, 24-hour specimen		.....	......	None		

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[5] Wien. med. Woch, 1882, xxxii, p. 214.

[6] Jour. Phar. and Exp. Therap., 1909, i, 39.

[7] Kratter, loc. cit.

[8] Hale, loc. cit.

[9] Vierteljahrschr. f. gerichtl. Med., 1892, iv, 15.

[10] Loc. cit.

During the earlier stages of the poisoning the amount of urine was diminished. When catheterized at 1.30 P.M., 123 c.c. were obtained, and we have no knowledge as to how much of this may have been excreted previous to the onset of the poisoning. At best not more than 23 c.c. per hour were excreted during this period, and it seems probable that very little urine was formed during the acute symptoms. According to Grützner[11] the constriction of the renal vessels during strychnine poisoning inhibits the flow of urine despite the increased blood pressure. The marked increase in the second portion of urine (58 c.c. per hour) was due mainly to the improved renal circulation, for the salt solution enema given forty minutes before this urine was obtained could hardly have been solely accountable for the considerable quantity of urine. The subsequent flood of urine was evidently due in part to the enemata and in part to the improved renal circulation.

During the acute stages of the poisoning very little strychnine was excreted, only 1 milligram having been obtained from the urine passed at 1.30 P.M. Had the patient died within two hours still smaller amounts, probably only traces, would have been recovered from the urine.

Following this period the excretion of strychnine increased rapidly, the maximum being reached between the hours of 6.25 P.M. and 11.30 P.M. during which period 49 milligrams were excreted, an average of almost 1 milligram per hour. The amount excreted diminished rapidly toward morning, the rate between 3.45 A.M. and 6.05 A.M. being less than 0.1 milligram per hour. During the second day no analyses were made. On the third day a distinct trace was obtained, and on the fourth a faint trace. On the fifth day no strychnine was obtained. Altogether, about 96 milligrams (1$\frac{3}{5}$ grains) were recovered from the urine. The analyses are noteworthy in showing (1) how little strychnine was excreted during the most acute stage of the poisoning, (2) that the major amount was excreted within twenty-four hours, and (3) that the excretion was not completed for three or four days.

But few observations on the effect of strychnine poisoning upon the body temperature of man are available. Observations on animals by Harnack,[12] Harnack and Hochheim,[13] Högyes,[14] Kionka,[15] and Rapmund,[16] indicate that, as a rule, the temperature rises during the convulsions and tends to fall between them. Indeed, in some instances the fall has predominated and the temperature was lowered throughout. Rapmund[17] records a rise from 39.1° to 42° C. on one dog, and several similarly large rises are on record.[18] Experiments by Kionka and by Harnack indicate that both the heat production and the heat elimination are increased, the resulting body temperature depending upon which of the two predominates. Harnack found that doses of strychnine which produced no convulsions might increase the heat production.

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[11] Arch. f. Physiol., 1875, xi, 385.

[12] Arch. exp. Path. u. Phar., 1903, xlix, 157.

[13] Zeitschr. f. klin. Med., 1894, xxv, 16.

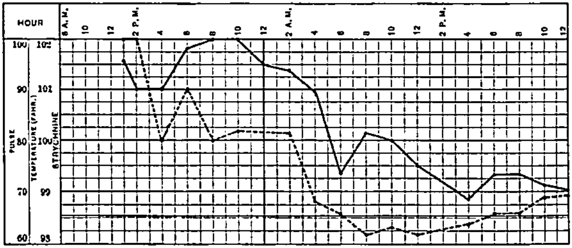
[14] Arch. f. exp. Path. u. Phar., 1881, xiv, 113.

[15] Abstract in Fortschr. d. Med., 1898, xvi, 941.

[16] Loc. cit.

[17] Loc. cit.

One hesitates to transfer these results to man, both because of the varying results obtained on animals and because of the finer temperature adjustment in man. Only occasional observations have been made upon the body temperature in cases of human poisoning with strychnine. Barthélemy[19] and Lesser[20] record normal temperatures. Habel's[21] patient, who took about 0.18 gram at 8.00 A.M., showed an evening temperature of 38° C., with subnormal temperatures on the following days. Honigmann's[22] patient showed a temperature of 38.1° C. twenty hours after taking the poison, and for several days his temperature ranged 38° and 38.4° C. (100.4° to 101.1° F.). He had an acute nephritis. In Ott's[23] patient the temperature rose to 101° F. on the first and second days, subsiding on the third day with rapid and complete convalescence. Wood states that he has never seen a temperature chart which showed fever after strychnine poisoning, nor have I been able to find a complete chart. The following chart is therefore of interest, since it shows a definite elevation of temperature for over twenty-four hours after taking the poisonous dose of the drug. Rectal temperatures were taken every two hours from 1.00 P.M. on the day of the poisoning to 4.00 A.M. on the following day, after which the temperature was taken in the axilla or by the mouth. These records show a marked and continued elevation of temperature, the highest being 102° F. It is



Temperature showing in continuous line; pulse in broken line. For the week previous the temperature had been 97.8° to 98.6° F., pulse 61 to 94.

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[18] Högyes, Loc. cit.

[19] Loc. cit.

[20] Deut. med. Woch., 1889, xv, 435.

[21] Ann. Hyg., 1885, xiii, 130.

[22] Münch. med. Woch., 1898, xlv, 7.

[23] Med. News, 1894, ii, 270.

noteworthy that all of these temperatures were taken after the severe convulsive stage had passed.

In animals both heat production and heat elimination are increased. One may judge the heat elimination in man roughly by the warmth of the extremities, the presence of perspiration, and the size of the peripheral pulse. During the early convulsive stage of the poisoning our patient had a very small radial pulse and the extremities were cool; but throughout the latter part of the first day the skin was warm and was covered with a moderate perspiration, while the radial pulse was unusually large; all of which characters we have learned to associate with a rapid rate of blood flow through the arm. Apparently, therefore, the body was eliminating heat in excessive quantities after the convulsive stage was over, and since its temperature remained elevated, it seems probable that the heat production was also markedly increased. When, however, we consider the fine adjustment of heat regulation in the normal individual and the rapidity with which any excessive heat produced in the body is eliminated, it is surprising that the elevation of temperature should have persisted for over twenty-four hours in our case, for two days in Ott's case, and for several days in Honigmann's case. One can hardly avoid the conclusion that strychnine poisoning may disturb the fine adjustment of heat regulation in the body, and that in a certain sense, we have a condition analogous to that which prevails in fever.

In conclusion I wish to thank Dr. V. C. Vaughan for his valuable suggestions and for the analyses which have made the case one of unusual interest.

INSUFFICIENCY OF THE PULMONARY VALVE.

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A student who wishes to investigate this subject will find himself indebted especially to four writers, Barié, Gerhardt, Gibson, and Pitt, and most of all to the first mentioned.

Barié[1] in the historical introduction to his paper reproduces a case reported by Morgagni[2] which is of great interest: "The patient was a young girl, sick and bedridden since birth, affected with peristent dyspnea and lividity of the skin. She died when sixteen years old. At the autopsy the right ventricle was found dilated, the pulmonary valves were cartilaginous, and so united as scarcely

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[1] Arch. gén. de méd., 1891.

[2] De Sedibus et Caus. Morborum, epist. 17, chap. 12, t. i, p. 359, trad. Destonet, 1837.